

Laparoscopic Management of Women with a Family History of Ovarian Cancer

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Background and Objective: The safety of laparoscopic surgery in women with a family history of ovarian cancer predicted to have benign disease has not been established. The objective of this study was to evaluate the feasibility and complications of operative laparoscopy and to describe the pathologic findings in this patient population.

Methods: Sixty-two consecutive women with a family history of ovarian cancer who elected prophylactic oophorectomy or had predicted benign adnexal disease were offered laparoscopic surgery. Patient characteristics, details of laparoscopic surgery, operative and postoperative complications, and histopathologic findings were recorded.

Results: Laparoscopy was converted to laparotomy in 2 patients (3.2%); 1 patient (1.6%) had an operative vascular complication, and 1 patient (1.6%) had postoperative bleeding. Median (range) estimated blood loss, operative time, and hospital stay were 50 ml (50–1,500), 120 min (60–290), and 1 day (0–9), respectively. Histopathologic findings included normal ovaries ($n = 20$), corpus luteum cyst ($n = 16$), follicular cyst ($n = 8$), endometriotic cyst ($n = 7$), serous cystadenoma ($n = 5$), epithelial hyperplasia ($n = 4$), dermoid cyst ($n = 1$), and fibrothecoma ($n = 1$).

Conclusions: Laparoscopic surgery is feasible and safe in women with a family history of ovarian cancer predicted to have benign disease and is associated with low blood loss and short hospital stay. Most ovaries removed are either normal or have benign disease.

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KEY WORDS: familial ovarian cancer; prophylactic oophorectomy; laparoscopy

INTRODUCTION

Family history of ovarian cancer is the most significant risk factor for ovarian cancer. Familial ovarian cancer constitutes about 7% of cases of ovarian cancer. Three hereditary familial cancer syndromes have been described: site-specific, breast or ovarian cancer syndrome, and hereditary nonpolyposis colorectal cancer syndrome, which includes colorectal cancer, endometrial cancer, ovarian cancer, and urologic cancers.

Secondary to cancer phobia, some women with a family history of ovarian cancer who have completed their families might elect prophylactic oophorectomy in the hope of avoiding ovarian cancer. Salpingo-oophorectomy performed through laparotomy could be associated with

significant postoperative pain, long hospitalization, and late recovery. On the other hand, the scope of operative laparoscopic surgery has greatly expanded over the last several years due to decreased postoperative pain, short hospitalization, and early recovery.

The role of laparoscopic surgery in the management of women with a family history of ovarian cancer has not been thoroughly studied. In a survey of the British Gynecological Cancer Society, members of the society felt that a family history of ovarian cancer should be consid-

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ered as a contraindication for operative laparoscopy [1]. On the other hand, little is known about ovarian histopathology in women with a family history of ovarian cancer and clinically normal ovaries or adnexal masses predicted to be benign. The aim of the present study was to evaluate the feasibility and complications of laparoscopic surgery in women with a family history of ovarian cancer with or without adnexal masses predicted to be benign and to describe the pathologic findings in these women.

MATERIALS AND METHODS

Sixty-two consecutive women with a family history of ovarian cancer with or without adnexal masses were offered laparoscopic surgery. These women were seen at the Department of Gynecologic Oncology at the Roswell Park Cancer Institute ($n = 54$) and at the Division of Gynecologic Oncology at the University of Vermont ($n = 8$) between June 1992 and September 1998. Patients suspected clinically to have ovarian cancer, patients with suspicious adnexal masses or adnexal masses larger than 10.0 cm, and patients with severe cardiovascular disease precluding laparoscopic surgery were excluded from the study and offered laparotomy. None of the patients were excluded on the basis of age or body mass index.

Patient characteristics including age, parity, menopausal status, height, weight, body mass index (weight in kilograms/ height in square meters), history of previous laparotomy, preoperative CA-125 (normal: 0–35 U/ml), and the ultrasound characteristics of adnexal masses if present were recorded. Details of the laparoscopic surgery were also recorded, including the operative procedure, estimated blood loss, operative time, presence and extent of adhesions, method of securing the infundibulopelvic ligament, operative complications, and the need to convert the procedure to laparotomy. Postoperative complications, length of hospitalization, and final histopathological diagnoses of the tissues retrieved at surgery were reported.

All laparoscopies were performed by the open technique. A 1-cm incision was made in the infraumbilical ridge, and the subcutaneous tissue was dissected until the rectus fascia was visualized. The rectus fascia was then grasped with two small Kocher clamps and incised. The parietal peritoneum was incised under direct vision. When access to the peritoneal cavity was gained, the Hasson cannula was inserted through the opening in the peritoneal cavity and anchored with vicryl sutures.

Pneumoperitoneum was then established using carbon dioxide. After the peritoneal cavity was distended and the inferior epigastric vessels were seen, a secondary and tertiary punctures (5 or 10 mm in diameter) were established in the right and left lower abdominal quadrants lateral to the inferior epigastric vessels. As a first step in

all surgical procedures, peritoneal washings were performed, and the fluid aspirated and sent for cytological evaluation. The infundibulopelvic ligaments were secured after visualization of the ureters. During the study period, three methods of securing the infundibulopelvic ligaments were utilized. The method was not randomized but dependent upon the surgeon's preference and availability of surgical supplies. The methods were bipolar cautery, laparoscopic stapler, and extracorporeal knot. Large adnexal masses were placed in an endobag, aspirated inside the bag, avoiding contamination of the peritoneal cavity, and then removed through a secondary or a tertiary puncture site. At the end of the surgical procedure and after evacuation of the pneumoperitoneum, all fascial incisions ≥ 1.0 cm were closed under direct vision using 0-vicryl sutures.

Estimated blood loss and operative time were taken from anesthesia records. Operative time was calculated from the start of the operative procedure to its end. Presence of adhesions was noted and graded as none, mild, moderate, or severe. Histopathological examination of tissues retrieved at surgery was performed by members of the Departments of Pathology at the Roswell Park Cancer Institute and the University of Vermont. Length of hospitalization was recorded as the day of discharge minus the day of the surgical procedure. Postoperative complications were divided into two groups: minor (if the complication did not result in unplanned admission, secondary surgical procedure, or blood transfusion) or major (if the complication resulted in unplanned admission, secondary surgical procedure, or blood transfusion).

Ultrasound examination of adnexal masses was recorded as normal, simple, or complex. Simple cysts were those described as completely cystic, unilocular, and with regular borders. Complex cysts included those that had a solid component, septae, or irregular borders. First-degree relatives were defined as parents, children, and siblings. Second-degree relatives were defined as grandparents, grandchildren, half-siblings, aunts, uncles, nieces, and nephews.

Statistical analysis was performed using Student's t -test for comparison of means and χ^2 test for comparison of proportions. Two-tailed $P < 0.05$ was considered significant.

RESULTS

Patient characteristics, indications for surgery, and details of the operative procedure are demonstrated in Tables I–III. Eight patients (12.9%) had body mass indices > 30.0 . Preoperative CA-125 values were elevated (> 35.0 U/ml) in 18 (29.0%) patients. The median CA-125 value in this group was 57 U/ml (range: 37–335 U/ml).

Laparoscopic surgery was successful in 60 patients (96.8%). The procedure was converted to laparotomy

TABLE I. Characteristics of Women with a Family History of Ovarian Cancer Who Underwent Laparoscopic Surgery

Characteristic	
No. of subjects	62
Age (years), median (range)	42 (27–75)
Height (m), median (range)	1.6 (1.5–1.81)
Weight (kg), median (range)	65.5 (45–141)
Body mass index, median (range)	24.4 (17.4–48.6)
Parity, median (range)	2 (0–6)
Menopause, no. (%)	
Postmenopausal	14 (22.6)
Premenopausal	48 (77.4)
Previous laparotomy, no. (%)	
None	34 (54.8)
One	13 (20.9)
Two	10 (16.1)
Three	5 (8.1)
CA-125 values, no. (%)	
Unknown	8 (12.9)
Normal	36 (58.1)
Elevated	18 (29.0)
Ultrasound appearance of the ovaries, no. (%)	
Not done	20 (32.3)
Normal	22 (35.5)
Simple cyst	14 (22.6)
Complex cyst	6 (9.7)

my in 2 patients because of dense adhesions that precluded visualization of the infundibulopelvic ligaments and the ureters. These 2 patients were 53 and 73 years old, their parities were 1 and 3, and their body mass indices were 32.4 and 22.6 (respectively); both of them were scheduled for laparoscopic bilateral salpingo-oophorectomy (BSO). Following laparotomy, the procedure was accomplished without complications. However, these two patients stayed for 7 and 9 days postoperatively because of postoperative fever and ileus.

One patient (1.6%) had a vascular intraoperative complication secondary to bleeding on opening the peritoneum of the broad ligament. The estimated amount of blood loss was 1,500 ml, and the patient was transfused 2 U of packed red blood cells. Postoperative complications were mild in 10 patients (16.1%) and major in 1 patient (1.6%). The latter patient had a 6-point postoperative drop in hematocrit that required transfusion of 2 U of packed red blood cells. It was judged that the patient had a retroperitoneal hematoma from one of the infundibulopelvic ligaments. The infundibulopelvic ligaments in that patient were secured using the laparoscopic stapler. Minor postoperative complications included fever ($> 38.0^\circ\text{C}$, $n = 6$), ileus ($n = 2$), urinary tract infection ($n = 1$), and urinary retention ($n = 1$).

The median postoperative stay following laparoscopic surgery was 1 day (range: 0–9). Hospital stay and operative and postoperative complications are listed in Table IV. As demonstrated in Table V, women who underwent laparoscopically assisted vaginal hysterectomy (LAVH) with BSO had significantly greater blood loss, longer

operative time, longer hospital stay, and more minor postoperative complications than those who underwent laparoscopic BSO (375.8 vs. 81.1 ml, $P < 0.005$; 191.8 vs. 121.4 min, $P < 0.005$; 2.7 vs. 1.3 days, $P < 0.05$; and 40.0% vs. 9.5%, $P < 0.001$, respectively). There were no long-term postoperative complications related to the procedures.

Pathologic findings of the removed ovaries included: normal ovaries ($n = 20$, 32.3%), corpus luteum cyst ($n = 16$, 25.8%), follicular cyst ($n = 8$, 12.8%), endometriotic cyst ($n = 7$, 11.2%), serous cystadenoma ($n = 5$, 8.0%), epithelial hyperplasia ($n = 4$, 6.4%), dermoid cyst ($n = 1$, 1.6%), and fibrothecoma ($n = 1$, 1.6%). Among patients who underwent LAVH/BSO, the pathologic findings were fibroid uterus ($n = 8$), adenomyosis ($n = 3$), uterine polyp ($n = 3$), and normal uterus ($n = 1$). None of the patients had unsuspected invasive cancer or borderline ovarian tumors. Peritoneal cytology demonstrated no malignant cells in all the patients. The most common ovarian pathology finding in our patient population was corpus luteum cyst. The most common pathology finding associated with elevated CA-125 was endometriotic cyst.

DISCUSSION

Women who have a family history of ovarian cancer face enormous psychological challenges: an increased risk of an often fatal disease, an earlier age of onset in successive generations [2], and a lack of a reliable screening test for the detection of early ovarian cancer. Faced with these challenges, some of these women might elect to undergo prophylactic oophorectomy.

Women with a family history of ovarian cancer considering prophylactic oophorectomy should be counseled that the procedure will not prevent a possible occurrence of primary peritoneal carcinoma [3] and that they will need postoperative long-term estrogen replacement therapy if the adverse effects of estrogen deprivation on bone and the cardiovascular system are to be avoided [4]. Despite recent reports of excellent compliance of this group of patients with estrogen replacement therapy [5], long-term effects of such therapy on the incidence of breast cancer remain controversial.

One of the factors worthy of consideration by this group of patients is the surgical approach to oophorectomy. The safety of laparoscopic oophorectomy in benign adnexal masses has been reported by several authors [6–9]. These reports have confirmed short hospitalization and early recovery following such a surgical approach. However, many gynecologists are reluctant to adopt a laparoscopic approach to the management of women with a family history of ovarian cancer. This reluctance is attributable to the facts that adnexal masses in such women are often considered suspicious, requiring management by laparotomy instead of laparoscopy, and that

TABLE II. Indications for Operative Laparoscopy in Women with a Family History of Ovarian Cancer

Indication	No. (%) (<i>n</i> = 62)
≥2 first-degree relatives with ovarian cancer	18 (29.0)
≥1 first- or second-degree relatives with ovarian cancer and ≥1 first- or second-degree relatives with breast cancer	4 (6.5)
Elevated CA-125 and adnexal mass	9 (14.5)
Adnexal mass	11 (17.7)
Elevated CA-125	9 (14.5)
Symptomatic uterine pathology	11 (17.7)

TABLE III. Details of Operative Laparoscopy in Women with a Family History of Ovarian Cancer*

	No. (%) (<i>n</i> = 62) ^a
Procedure	
Bilateral salpingo-oophorectomy	42 (58.1) ^b
Unilateral salpingo-oophorectomy	4 (6.5)
Ovarian cystectomy	1 (1.6)
LAVH/BSO	15 (24.2) ^c
Estimated blood loss (ml), median (range)	50 (50–1,500)
Adhesions	
None	38 (61.3)
Mild	8 (12.9)
Moderate	9 (14.5)
Severe	7 (11.3)
Securing the infundibulopelvic ligament	
Extracorporeal knot	12 (19.4)
Stapler	34 (54.8)
Cautery	14 (22.6)
Combination of two of the above	2 (3.2)
Operative time (min), median (range)	120 (60–290)

*LAVH/BSO: laparoscopically assisted vaginal hysterectomy with bilateral salpingo-oophorectomy.

^aUnless specified as median (range).

^bEight and ^c3 of these patients had lysis of adhesions as well.

the safety of laparoscopic surgery in such patient population has not been clearly demonstrated. Recently, Menczer et al. [10] reported on 4 women with a family history of ovarian cancer who underwent laparoscopic prophylactic oophorectomy. These authors confirmed that the procedure was of short duration, was uncomplicated, and required only brief hospitalization.

Recently, genetic linkage analyses have revealed that the majority of breast and ovarian cancer families are linked to the BRCA1 gene, while some cases of hereditary ovarian cancer are also apparent in breast cancer families linked to the BRCA2 gene [11]. With the ability to identify inherited mutations in BRCA1 and BRCA2, prophylactic oophorectomy and mastectomy can be offered specifically to women carrying such mutations. Grann et al. [12] investigated the value of prophylactic oophorectomy and mastectomy in young Ashkenazi Jewish women carrying BRCA1 or BRCA2 mutant genes. Using a Markov model, these authors demonstrated that for a 30-year-old woman, according to her cancer risks, prophylactic oophorectomy improved survival by 0.4 to

TABLE IV. Hospital Stay and Operative and Postoperative Complications Among Women with a Family History of Ovarian Cancer Who Underwent Laparoscopic Surgery

	No. (%) (<i>n</i> = 62) ^a
Hospital stay (days)	
Median (range)	1 (0–9)
>3 days	6 (9.7)
Operative complications	
Excessive blood loss	1 (1.6)
Postoperative complications	
Major	
Significant drop in hematocrit	1 (1.6)
Minor	
Fever (>38.0°C)	6 (9.7)
Atelectasis	3 (4.8) ^b
Ileus	2 (3.2)
Urinary tract infection	1 (1.6)
Urinary retention	1 (1.6)

^aUnless specified as median (range).

^bThese 3 patients also had fever.

2.6 years; mastectomy, by 2.8 to 3.4 years; and mastectomy and oophorectomy, by 3.3 to 6.0 years over surveillance. In another study of women with BRCA1 or BRCA2 mutations, Schrag et al. [13], using decision analysis, calculated that prophylactic oophorectomy and prophylactic mastectomy prolong life expectancy of a 30-year-old woman by 0.3–1.7 and 2.9–5.3 years, respectively, depending on the cumulative risk of cancer. However, our knowledge of the clinical significance of BRCA1 and BRCA2 mutations is still evolving and an optimal strategy for management of women with a family history of ovarian cancer based on these tests remains to be established.

Several investigators have examined ovaries removed prophylactically from women with a family history of ovarian cancer in hopes of identifying early premalignant changes. Werness et al. [14] compared ovaries removed prophylactically from women with a family history of ovarian cancer with those from age-matched women without such history by using light microscopy and computerized image cytometry. These authors demonstrated that ovaries removed prophylactically from women with a family history of ovarian cancer demonstrated subtle changes identifiable on image cytometry. None of the

TABLE V. Comparison Between Laparoscopic Bilateral Salpingo-Oophorectomy (BSO) and Laparoscopically Assisted Vaginal Hysterectomy (LAVH) with BSO in 57 of 62 Women with a Family History of Ovarian Cancer

	BSO	LAVH/BSO	P*
Number	42	15	
Estimated blood loss (ml)	81.1 ± 81.1	375.8 ± 374.2	<0.005
Operative time (minutes)	121.4 ± 36.1	191.8 ± 54.1	<0.005
Operative complications	0	1 (1.6%)	NS
Procedure converted	2 (3.2%)	0	NS
Hospital stay (days)	1.3 ± 1.3	2.7 ± 1.7	<0.05
Postoperative complications, no. (%)			
Major	1 (1.6)	0	NS
Minor	4 (9.5)	6 (40.0)	<0.001

*Statistical analysis was performed using Student's *t*-test and χ^2 . NS: not significant.

patients in the current study had ovarian cancer or borderline ovarian tumors. This is explained by the fact that women with a family history of ovarian cancer suspected of having ovarian cancer were managed by laparotomy. All the women included in the current study were predicted to have normal ovaries or benign disease. We found that the most common etiology of an adnexal mass and elevated CA 125 in our study group was endometrial cysts.

The present study attests to the safety of operative laparoscopy in the management of women with a family history of ovarian cancer predicted to have normal ovaries or benign disease. We think that the low incidence of operative complications reported here is partially attributable to our adoption of the open laparoscopic technique and closure of all fascial incisions ≥ 1 cm. The open laparoscopic technique avoids bowel and vascular injury secondary to the blind insertion of the trocar and cannula. Closure of fascial incisions ≥ 1 cm avoids bowel herniation through such incisions. As expected, patients undergoing LAVH/BSO had significantly longer operative procedures, more blood loss, longer hospital stay, and more minor postoperative complications than those undergoing laparoscopic BSO. However, there was no significant increase in operative or major postoperative complications between these two groups. The short operative time, low blood loss, and short hospital stay reported in our study support the contention that laparoscopic surgery is worthy of consideration in such a group of women. The results of the current study should not be interpreted as a blanket endorsement for prophylactic oophorectomy. Such a decision should be considered carefully and thoroughly after discussion of the pros and cons with the patient considering the procedure.

CONCLUSIONS

Laparoscopic surgery is feasible and safe in women with a family history of ovarian cancer predicted to have

benign disease and is associated with low morbidity and short hospitalization. In this patient population, most ovaries removed are either normal or have benign disease.

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